REMARKS

Claims 1-5 are pending in the instant application. Claims 1-5 have been rejected. Claims 1-5 have been amended. No new matter has been added by these amendments to the claims. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims 1-5 under 35 U.S.C. § 112, second paragraph

Claims 1-5 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner suggests that claims 1-5 are vague and indefinite in the recitation of "complement" as the Examiner suggests that it is not clear whether or not the complement should include several nucleic acid base pairs, partial length or a full-length complement.

In addition, the Examiner suggests that the recitation "hybridizing under stringent conditions" in claims 1-5 is vague and indefinite.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claims 1-5 to remove the term "complement".

With respect to the suggested indefiniteness of the recitation of "hybridizing under stringent conditions", however, Applicants respectfully disagree with the Examiner.

In accordance with MPEP § 2173, the primary purpose of the requirement of definiteness of claim language is to ensure that the scope of the claimed is clear so that the public is informed of the boundaries of what constitutes infringement of the patent. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

(A) The content of the particular application disclosure;

(B) The teachings of the prior art; and

(C) The claim interpretation that would be given by one possessing the ordinary level of skill in that pertinent art at the time the invention was made. Only a reasonable degree of particularly and distinctness is required. MPEP § 2173.01. Further, the MPEP and the case law are clear; when reviewing a claim for compliance with 35 U.S.C. § 112, second paragraph, the Examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope

and, therefore, serves the notice function required by 35 U.S.C. § 112, second paragraph.

Claims of the instant application are drawn to methods for determining levels of a colon specific gene(CSG) comprising a polynucleotide sequence of SEQ ID NO:1 or a polynucleotide which hybridizes under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, in cells, tissues or bodily fluids in a patient.

Methods for assessing whether a polynucleotide hybridizes under stringent conditions are well known to those of skill in the art and set forth in great detail in standard reference texts such as Sambrook et al. 1989 (Molecular Cloning, A Laboratory Manual, 2nd Edition, Cold Spring Harbor Press, Cold Spring Harbor). Such methods can be performed routinely by those of skill in the art to assess whether or not a polynucleotide from a cell, tissue of bodily fluid of a patient hybridizes under stringent conditions to SEQ ID NO:1 and thus falls within the scope of the claimed method.

Further, definitions from two online dictionaries which were available prior to the filing date of the instant application for the term hybridization stringency are also being provided herewith. Both definitions require that the percentage of matching nucleotides be 70% or greater for stringent hybridization to occur.

Prior art cited by the Examiner under 35 U.S.C. § 102(b) and (e) also requires 70% identity for hybridization and greater than 70% identity for stringent hybridization. See specifically, col. 6, lines 10-14, of U.S. Patent 5,733,748, and page 10 of WO 96/39419. Accordingly, one of skill in the art can also routinely assess whether or not a polynucleotide falls within the scope of the present invention by determining whether the sequence has 70% or greater identity with SEQ ID NO:1.

Thus, the claims, as amended are definite when read in light of the teachings of the prior art and what is well known by those of skill in the art. Further, the claims when read as a whole apprise one of ordinary skill in the art of their scope, thus meeting the requirements of 35 U.S.C. § 112, second paragraph.

Withdrawal of this rejection under 35 U.S.C. § 112, first paragraph is therefore respectfully requested.

II. Rejection of Claims 1-5 under 35 U.S.C. § 102(e) and 102(b)

Claims 1-5 have been rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent 5,733,748. The Examiner suggests that this patent teaches a CSG comprising a polynucleotide sequence that would hybridize under stringent conditions with SEQ ID NO: 1 of the instant application.

Claims 1-5 have also been rejected under 35 U.S.C. § 102(b) as being anticipated by WO 96/39419 as the Examiner suggests that this reference teaches a polynucleotide sequence with the sequence GCT, which would also hybridize under stringent conditions with SEQ ID NO:1.

Applicants respectfully disagree as these rejections are based upon the scientifically erroneous suggestion that a polynucleotide with one or two sections of only three continuous bases of complementarity would hybridize under stringent conditions to SEQ ID NO:1. The complementarity requirements for hybridization under stringent conditions are well known to those of skill in the art and far exceed the complementarity between the sequence taught in U.S. Patent 5,733,748 or WO 96/39419 and SEQ ID NO: 1 of the instant application.

In fact, both prior art references cited in this rejection teach that polynucleotides hybridize if there is at least 70%, preferably at least 90% and more preferably at least 95% identity between the sequences. See specifically, col. 6, lines 10-14, of U.S. Patent 5,733,748, and page 10 of WO 96/39419. Accordingly, the Examiner's suggestion that the sequence taught in these references will hybridize under stringent conditions to SEQ ID NO:1

of the present invention actually contradicts with the teachings of these cited prior art references.

MPEP § 2111.01 is quite clear; the words of a claim must be given their plain meaning unless they are defined in the specification. Plain meaning, as set forth in MPEP § 2111.01 refers to the meaning given to the term by those of ordinary skill in the art. The meaning given by those of skill in the art to the term stringent hybridization with respect to polynucleotides is a sequence with at least 70% identity or greater. This accepted meaning is evidenced not only by the prior art references cited by the Examiner in this rejection but also by dictionary definitions of the term published prior to the filing date of the instant application. Copies of dictionary definitions for hybridization stringency from two different online sources are provided herewith. In both definitions it is stated that if the percentage of matching nucleotide is lower than 70%, the two single-stranded nucleic acid molecules are considered nonhomologous and any hybridization is considered non-stringent.

The sequence taught by U.S. Patent 5,733,748 and WO 96/39419 has less than 70% identity with SEQ ID NO:1 and thus, in accordance with the teachings of both U.S. Patent 5,733,748 and WO 96/39419 would not hybridize with SEQ ID NO:1. Accordingly, these

references do not enable a polynucleotide which hybridizes under stringent conditions with SEQ ID NO:1 and therefore cannot anticipate a claim wherein the polynucleotide hybridizes under stringent conditions to SEQ ID NO:1.

Withdrawal of these rejections under 35 U.S.C. § 102(e) and § 102(b) is therefore respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."

Respectfully submitted,

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Date: **November 4, 2002**

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

1. (amended) A method for diagnosing the presence of colon cancer in a patient comprising:

(a) determining levels of a colon specific gene(CSG) comprising a polynucleotide sequence ~~or its complement capable of hybridizing~~ of SEQ ID NO:1 or a polynucleotide which hybridizes under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, in cells, tissues or bodily fluids in a patient; and

(b) comparing the determined levels of the CSG with levels of the CSG in cells, tissues or bodily fluids measured in a normal human control, wherein a change in determined levels of the CSG in said patient versus levels of the CSG measured in a normal human control is associated with the presence of colon cancer.

2. (amended) A method of diagnosing metastases of colon cancer in a patient comprising:

(a) identifying a patient having colon cancer that is not known to have metastasized;

(b) determining levels of a colon specific gene(CSG) comprising a polynucleotide sequence ~~or its complement capable of hybridizing~~ of SEQ ID NO:1 or a polynucleotide which hybridizes under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, in cells, tissues or bodily fluids in a patient; and

(c) comparing the levels of the CSG determined in step (b) with levels of the CSG measured in a sample of cells, tissues or bodily fluid from a normal human control, wherein an increase in levels of the CSG determined in step (b) as compared to levels of the CSG measured in a sample of cells, tissues or bodily fluid from a normal human control is associated with a cancer that has metastasized.

3. (amended) A method of staging colon cancer in a patient having colon cancer comprising:

(a) identifying a patient having colon cancer;

(b) determining levels of a colon specific gene(CSG) comprising a polynucleotide sequence ~~or its complement capable of hybridizing~~ of SEQ ID NO:1 or a polynucleotide which hybridizes under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, in cells, tissues or bodily fluids in a patient; and

(c) comparing the levels of the CSG determined in step (b) with levels of the CSG measured in a sample of cells, tissues or bodily fluid from a normal human control, wherein an increase in the levels of the CSG determined in step (b) as compared to levels of the CSG measured in a sample of cells, tissues or bodily fluid from a normal human control is associated with a cancer that is progressing and a decrease in the levels of the CSG determined in step (b) as compared to levels of the CSG measured in a sample of cells, tissues or bodily fluid from a normal human control is associated with a cancer that is regressing or in remission.

4. (amended) A method of monitoring colon cancer in a patient for the onset of metastasis comprising:

(a) identifying a patient having colon cancer that is not known to have metastasized;

(b) periodically determining levels of a colon specific gene(CSG) comprising a polynucleotide sequence ~~or its complement capable of hybridizing~~ of SEQ ID NO:1 or a polynucleotide which hybridizes under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, in cells, tissues or bodily fluids in a patient; and

(c) comparing the periodically determined levels of the CSG with levels of the CSG measured in cells, tissues or bodily

fluid of a normal human control, wherein an increase in any one of the periodically determined levels of the CSG in the patient versus the normal human control is associated with a cancer that has metastasized.

5. (amended) A method of monitoring a change in stage of colon cancer in a patient comprising:

(a) identifying a patient having colon cancer;

(b) periodically determining levels of a colon specific gene(CSG) comprising a polynucleotide sequence ~~or its complement capable of hybridizing~~ of SEQ ID NO:1 or a polynucleotide which hybridizes under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, in cells, tissues or bodily fluids in a patient; and

(c) comparing the periodically determined levels of the CSG with levels of the CSG measured in cells, tissues, or bodily fluid of a normal human control, wherein an increase in any one of the periodically determined levels of the CSG in the patient versus the normal human control is associated with a cancer that is progressing in stage and a decrease is associated with a cancer that is regressing in stage or in remission.

hybridisation stringency

<molecular biology> The percentage of nucleotides which must match on two unrelated single-stranded nucleic acid molecules before they will base pair with each other to form a duplex, given a certain set of physical and chemical conditions.

The hybridisation stringency is used to determine when a hybridisation probe and a target nucleic acid will come together, and can be set by the researcher by varying the conditions. In general, if the percentage of matching nucleotides is lower than 70 percent, the two single-stranded nucleic acid molecules are considered nonhomologous and any hybridisation is considered nonstringent.

(13 Oct 1997)

Previous: hybrid DNA, hybrid dysgenesis, hybrid enzyme, hybrid inviability, hybridisation
Next: hybridism, hybridization, hybrid molecule, hybrid name, hybridoma

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LIFE SCIENCE DICTIONARY

Search Results

Search Terms: AND Search Definitions:

Contains this Begins with this

Find Words! Clear Form

Searching Category	User input query
Searched Word	hybridization
Number of Results	14

1. 1. **colony hybridization**
   Definition:
   A genetics lab technique used to identify which colonies of bacteria on an agar plate contain a particular sequence of DNA or a particular gene. The technique involves pressing a nylon or nitrocellulose membrane onto the plate so that each colony contributes a small smudge of itself to the membrane, then treating the membrane with chemicals and heat, then washing the membrane with a labeled probe to find the specific DNA sequence. The smudges which are indicated by the probe are then compared back to the colonies on the agar plate. This technique is often used in conjunction with experiments involving the making of genomic libraries.

2. **competition hybridization**
   Definition:
   A lab technique used to determine how similar two strands of single-stranded nucleic acids are to each other by putting them with a third strand (called a standard) and observing how well they can bond with each other to become double-stranded (how well they hybridize).

3. **cross-hybridization (cross hybridization)**
   Author: Susan A.Hagedorn
   Definition:
   The hydrogen bonding of a single-stranded DNA sequence that is partially but not entirely complementary to a single-stranded substrate. Often, this involves hybridizing a DNA probe for a specific DNA sequence to the homologous sequences of different species.

4. **DNA hybridization**
   Definition:
   A lab technique used to find out how closely related two or more separate strands of DNA from different species are to each other. The technique involves radioactive labeling.

5. **DNA-RNA hybridization**

Definition:

A type of hybridization. In this case, a strand of DNA is joined with a complementary strand of RNA to form a double-stranded molecule (or one which is partly double-stranded, if one of the original single strands is shorter than the other).

6. **FISH (fluorescence in situ hybridization)**

Definition:

A physical mapping approach that uses fluorescent tags to detect hybridization of probes with metaphase chromosomes and with the less-condensed somatic interphase chromatin.

7. **hybridization**

Definition:

1. The process of joining two complementary strands of DNA or one each of DNA and RNA to form a double- stranded molecule.
2. The mating of individuals from different species or sub-species.

8. **hybridization stringency**

Definition:

The percentage of nucleotides which must match on two unrelated single-stranded nucleic acid molecules before they will base pair with each other to form a duplex, given a certain set of physical and chemical conditions. The hybridization stringency is used to determine when a hybridization probe and a target nucleic acid will come together, and can be set by the researcher by varying the conditions. In general, if the percentage of matching nucleotides is lower than 70 percent, the two single-stranded nucleic acid molecules are considered nonhomologous and any hybridization is considered nonstringent.

9. **in situ hybridization**

Definition:

Use of a DNA or RNA probe to detect the presence of the complementary DNA sequence in cloned bacterial or cultured eukaryotic cells.

Also used for locating genes on chromosomes. The process is:

1. Prepare microscope slide with cells in metaphase of mitosis.
2. Treat slide with a weak base. Thus denaturing the DNA.
3. Pour radioactively labeled probe onto the slide.
4. Expose slide to photographic emulsion for a few days or weeks.
5. Develop emulsion.

10. **introgressive hybridization**

Definition:

The incorporation into a population's gene pool of genes from a different species.

11. **Northern blot (Northern hybridization, Northern blotting)**

Definition:

A technique similar to Southern blotting, though it is used for RNA. In this technique, RNA fragments are transferred from an agarose gel to a nitrocellulose filter, where the RNA is then hybridized to a radioactive probe.

12. **probe (hybridization probe)**
Definition:

A single-stranded nucleic acid molecule with a known nucleotide sequence which is labeled in some way (for example, radioactively, fluorescently, or immunologically) and used to find and mark certain DNA or RNA sequences of interest to a researcher by hybridizing to it.

13. **Southern blot (Southern hybridization, Southern blotting)**
Definition:

A technique used for searching for a specific DNA fragment. The process is as follows:

1. Separate DNA fragments by gel electrophoresis
2. change pH of gel to basic, thus allowing disruption of H-bonds
3. blot gel with nitrocellulose paper
4. heat paper so as to fix DNA fragments
5. probe with labeled messenger RNA or cDNA
6. wash
7. complementary mRNA/cDNA fragments will have hybridized.

14. **Western blot (Western hybridization, Western blotting)**
Definition:

A technique similar to Southern blotting, though it is used for proteins.

END